REMARKS/ARGUMENTS

Claims 122-126 and 129-131 are pending in this application. The rejections to the presently pending claims are respectfully traversed.

Claim Rejections – 35 U.S.C. §101 and §112, First Paragraph

Claims 122-126 and 129-131 are rejected under 35 U.S.C. §101 allegedly "because the claimed invention is not supported by either a specific, substantial asserted utility or a well established utility." (Page 2 of the instant Final Office Action). Claims 122-126 and 129-131 are further rejected under 35 U.S.C. §112, first paragraph, allegedly "since the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility, one skilled in the art would not know how to use the claimed invention." (Page 3 of the instant Final Office Action). Applicants respectfully disagree with and traverse these rejections.

The Examiner asserts that since the protein of the invention is not supported by a specific and substantial asserted utility or well established utility, the encoding polynucleotides, chimeric proteins also lack utility.

Utility Guidelines

According to the Utility Examination Guidelines ("Utility Guidelines"), 66 Fed. Reg. 1092 (2001) an invention complies with the utility requirement of 35 U.S.C. §101, if it has at least one asserted "specific, substantial, and credible utility" or a "well-established utility."

Under the Utility Guidelines, a utility is "specific" when it is particular to the subject matter claimed. For example, it is generally not enough to state that a nucleic acid is useful as a diagnostic without also identifying the conditions that is to be diagnosed.

The requirement of "substantial utility" defines a "real world" use, and derives from the Supreme Court's holding in *Brenner v. Manson*, 383 U.S. 519, 534 (1966) stating that "The basic *quid pro quo* contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility." In explaining the "substantial utility" standard, M.P.E.P. §2107.01 cautions, however, that Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar formulations used in certain court decisions to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement. "Rather,

any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient, at least with regard to defining a "substantial" utility." (M.P.E.P. 2107.01, Emphasis added.). Indeed, the Guidelines for Examination of Applications for Compliance with the Utility Requirement, set forth in M.P.E.P, §2107 II(B)(1) gives the following instruction to patent examiners: "If the (A)pplicant has asserted that the claimed invention is useful for any particular practical purpose . . . and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility."

Finally, the Utility Guidelines restate the Patent Office's long established position that any asserted utility has to be "credible." "Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record . . . that is probative of the Applicant's assertions." (M.P.E.P. §2107 II(B)(1)(ii)). Such standard is presumptively satisfied unless the logic underlying the assertion is seriously flawed, or if the facts upon which the assertion is based are inconsistent with the logic underlying the assertion (Revised Interim Utility Guidelines Training Materials, 1999).

To overcome the presumption of truth based on an assertion of utility by the Applicant, the Examiner must establish that **it is more likely than not** that one of ordinary skill in the art would doubt the truth of the statement of utility. **Absolute predictability is not a requirement.**

Only after the Examiner has made a proper *prima facie* showing of lack of utility, does the burden of rebuttal shift to the Applicant. The issue will then be decided on the totality of evidence.

Arguments

The Examiner has relied on the teaching of Pennica *et al.,* Alberts and Lewin *et al.,* Meric *et al.,* Futcher *et al.,* Hu *et al.,* Orntoft *et al.,* Godbout *et al.,* to support his position that "theoretical correlation of mRNA with protein is not probative" (Page 4 of the instant Final Office Action). The Examiner further alleges " The fact that needs to be established here is that a ΔCt value of at least 1.0 would be predictive of increased protein expression." (Page 4 of the instant Final Office Action).

Applicants first respectfully point out that the observed increase in PRO809 gene amplification in lung tumor is **significant**, as was discussed in detail in the previous responses and in the Appeal Brief filed December 22, 2005. Applicants have repeatedly argued that gene amplification, an essential mechanism for oncogene activation, is well-described in Example 170, page 539 onwards of the present application. Gene amplification was monitored using real-time quantitative TaqMan™ PCR and the results are set forth in Table 9B. As explained in the passage on page 539, lines 37-39, "the results of TaqMan™ PCR are reported in ΔCt units. **One unit** corresponds to one PCR cycle or approximately a **2-fold amplification**, relative to control, two units correspond to 4-fold, 3 units to 8-fold amplification and so on." (Emphasis added). Applicants show that PRO809 showed approximately 1.05-1.61 ΔCt units which corresponds to $2^{1.05}$-$2^{1.61}$- fold amplification or **2.070 to 3.053-fold** amplification in lung tumors, which is significant and thus the PRO809 gene has utility as a diagnostic marker of human lung cancer.

Further, Applicants have submitted over a hundred references with their Preliminary Amendment filed July 5, 2006, which collectively teach that, in general, there is a correlation between mRNA levels and polypeptide levels.

Pennica *et al.*

Yet, the Examiner maintains that "[t]here is strong opposing evidence showing that gene amplification is not predictive of increased mRNA levels in normal and cancerous tissue".(Page 4 of the instant Final Office Action). The Examiner repeats her rejection based on Pennica *et al.*

Applicants have previously argued this point in detail, in the previous responses and in the Appeal Brief filed December 22, 2005. These arguments are hereby incorporated by reference, and are not repeated here for brevity.

Alberts and Lewin

While acknowledging that the teachings of Alberts and Lewin that the initiation of transcription is the most common point for a cell to regulate the gene expression, the Examiner asserts that the initiation of transcription is not the only means of regulating gene expression according to the teaching of Alberts. (Page 6 of the instant Final Office Action).

Applicants respectfully disagree and submit that the utility standard is not **absolute certainty**. Rather, to overcome the presumption of truth that an assertion of utility by an applicant enjoys, the PTO must establish that it is **more likely than not** that one of ordinary skill in the art would doubt the truth of the statement of utility. Therefore, Applicants **do not need** to establish that the transcription initiation is **the only means** of regulating gene expression in order to meet the utility standard. Instead, as long as it is the most common point of regulation, as admitted by the Examiner, it would be more likely than not that a change of the transcription level of a gene gives rise to a change in translation level of a gene. Thus, the utility standard is met.

Meric *et al*

With respect to Applicants' arguments on Meric *et al.*, the Examiner asserts that Meric teaches that the gene expression is quite complicated, and is also regulated at the level of mRNA stability, mRNA translation, and protein stability. (Pages 7 of the instant Final Office Action).

Applicants emphasize that it is not a legal requirement to establish an absolute correlation between an increase in the mRNA level and protein expression levels that would correlate to the disease state nor is it imperative to find evidence that protein levels can be accurately predicted. Therefore, the Examiner has misinterpreted the teaching of Meric and applied improperly high legal standard.

Applicants respectfully submit that Meric simply summarizes the translation regulation of cancer cells. Meric indicates that translation initiation is regulated in response to nutrient availability and mitogenic stimulation and is coupled with cell cycle progression and cell growth. Meric further discusses that alteration in translation control occur in cancer. For example, variant mRNA sequences can alter the translational efficiency of individual mRNA molecule. (see Abstract). Meric further teaches that the changes of the translational efficiency of a mRNA transcript depend on the mutation of a specific mRNA sequence. (Page 973, column 2 to page 974, column 1). Meric never suggest that the translation of a cancer gene is suppressed in cancer in general, and therefore, an increased mRNA levels will not yield an increased protein levels. To the contrary, Meric teaches that the translation efficiency of a number of cancer genes is enhanced in cancer cells compared to its normal counterpart. For instance, in patient with

multiple myeloma, a C-T mutation in the c-myc IRES was identified and found to cause an enhanced initiation of translation. (Page 974, column 1). Therefore, the level of proteins encoded by these genes increases in cancer cells at an even higher magnitude than the mRNA level. As absolute accurate prediction of the protein level based on the mRNA level should not be required, the Examiner has failed to establish a *prima facie* showing of lack of utility in this instance.

Futcher *et al.*

The Examiner further asserts regarding the newly cited references by the Applicant, with the exception of Futcher *et al.*, that they are directed to the analysis of single genes, or a small group of genes, and therefore do not demonstrate trends found across proteins in general. (Page 7 of the instant Final Office Action). The Examiner further relies on previously cited and discussed Hu *et al.*, to reiterate this position.

Applicants have already discussed the Hu *et al.*, reference in the Appeal brief filed December 22, 2005. These arguments are hereby incorporated by reference, and are not repeated here for brevity.

Applicants note that the previously submitted 148 references support the notion that there is a general correlation between the change of mRNA levels of a gene and the change in protein expression levels of the gene. This is well-accepted in the art regardless how mRNA and protein are measured, for example, whether microarray is used to measure mRNA levels. Subsequently, the fact that many submitted references measure mRNA with assays other than microarray does not mitigate the existence of mRNA/protein correlation. On the contrary, it exactly confirms that such a correlation is observed when varied experimental methods are used.

Applicants further note that the submitted references, which represent the experiments conducted by a large number of different study groups, exactly demonstrate a trend of correlation found across proteins in general, because this trend is confirmed by overwhelming amount of experiments by different researchers, using diverse experimental designs, testing various types of tissues at numerous biological conditions. Although only a single gene or a small group of genes was tested by an individual study group, the cumulative evidence by over one hundred study

groups certainly establishes that it is well-accepted in the art that a general mRNA/protein correlation exists.

Orntoft *et al.*

The Examiner maintains that the Orntoft *et al.*, reference is not persuasive because Specification's disclosure are not characterized on the basis of those in the Orntoft *et al.* publication. (Page 7 of the instant Final Office Action).

The Orntoft reference was submitted by the Applicants with their Response of November 4, 2004, was discussed in detail therein, and was further discussed in the Appeal Brief filed December 22, 2005. These arguments are hereby incorporated by reference, and are not repeated here for brevity.

Orntoft was submitted to show that there was a gene dosage effect and teaches that "in general (18 of 23 cases) chromosomal areas with more than 2-fold gain of DNA showed a corresponding increase in mRNA transcripts" (see column 1, abstract). Based on this reference and on several other references submitted in the IDS filed with the last response, Applicants have submitted that it is generally well-understood in the art that DNA copy number influences gene expression. For example, Orntoft *et al.* studied transcript levels of 5600 genes in malignant bladder cancers which were linked to a gain/loss of chromosomal material using an array-based method.

Applicants submit that the DNA encoding PRO809 would have utility even if it were shown not to be in a gene cluster, because the instant specification has already determined that the PRO809 DNA is amplified significantly compared to its control. Applicants have provided an expert Declaration (the Goddard Declaration) to support the significance of the values obtained in the gene amplification assay for PRO809 DNA. Therefore, a utility rejection based on the premise that PRO809 DNA may not be within an amplified cluster is not appropriate according to the utility standards.

Godbout *et al.* and Bea *et al.*

With respect to the over one hundred additional references cited in Applicants' Preliminary Amendment filed on July 5, 2006, the Examiner asserts that only a single reference,

that by Godbout *et al.*, is relevant to the issue of whether gene amplification is correlated with increased mRNA and protein expression levels. (Page 8 of the instant Final Office Action).

Applicants have acknowledged that the new references submitted in the Information Disclosure Statement filed on July 5, 2006, focus on the correlation between mRNA expression and protein expression levels, and for the most part do not examine gene amplification. However, those few references that actually looked at gene amplification **did** find a correlation between gene amplification and increased mRNA and protein expression levels. Applicants further respectfully submit that, as discussed in the Preliminary Amendment filed on July 5, 2006, Bea *et al.* investigated gene amplification, mRNA expression, and protein expression of the putative oncogene BMI-1 in human lymphoma samples, and supports Applicants' assertion that gene amplification is correlated with both increased mRNA and protein expression.

The Examiner further asserts that Godbout *et al.* teaches that "co-amplified genes are only over-expressed if they provide a selective growth advantage to the cells." (Page 9 of the instant Final Office Action). Applicants respectfully submit that the passage cited by the Examiner is based upon two references from 1987 and 1992. In contrast, Applicants have made of record three more recent references, published in 2002, by Orntoft *et al.*, Hyman *et al.*, and Pollack *et al*, (made of record in Applicants' Response filed on November 4, 2004), which collectively teach that in general, gene amplification increases mRNA expression. Applicants submit that these more recent references must be acknowledged as more accurately reflecting the state of the art regarding the correlation between gene amplification and transcript expression than the references cited by Godbout *et al.*

The Examiner asserts that, "It is not disclosed, and based upon the sequence searches in this case, the Examiner cannot find any reason to suspect, that the protein encoded by the PRO809 gene would confer any selective advantage on a cell expressing it. It has no known homology to an RNA helicase or any other protein that would be expected to confer a selective advantage to a tumor cell. (Page 9 of the instant Final Office Action).

First of all, Applicants submit that the cited reference, Godbout *et al.*, was presented as evidence to support the existence of a general correlation between genomic DNA amplification and protein expression. Applicants have asserted utility for PRO809 as a novel tumor marker based on its positive result in the gene amplification assay.

In this rejection, the Examiner contemplates an explanation for 'how PRO809 confers selective advantages to the tumor cell;' in other words, on the mechanism by which PRO809 acts. That is, rather than focusing on the positive result itself, the Examiner seems to focus on the mechanism of action. However, knowledge of the mechanism is not relevant, nor required for the claimed invention to be useful. In fact, as stated by the Federal Circuit, "it is not a requirement of patentability that an inventor correctly set forth, or even know, how or why the invention works." *In re Cortwright*, 165 F.2d 1353, 1359 (Fed. Cir. 1999). The Federal Circuit has also stated that "[a]n invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is not operable in certain applications is not grounds for finding lack of utility." *Envirotech Corp. v. Al George, Inc.* 730 F.2d 753,762, 221 USPQ 473,480 (Fed. Cir. 1984)."

Moreover, as the Examiner is aware, there are many pathways to tumorigenesis, and screening for novel diagnostic tumor markers is routine in the art. Even for the identification a tumor marker, a showing of homology to other known tumor proteins (like RNA helicase) is not required. For this additional reason, the Examiner's concerns are misplaced, and should be withdrawn.

Applicants respectfully submit that, as discussed in the previously filed Preliminary Amendment and in the instant Response, none of the references cited by the Examiner suffices to establish a lack of general correlation between changes in genomic DNA amplification of a gene and changes in its corresponding protein expression level. On the other hand, Applicants have provided an overwhelming amount of evidences supporting the existence of a genomic DNA amplification/protein correlation. Accordingly, the evidences of the record have already established that it is "more likely than not" that increased genomic DNA amplification to predict increased protein levels.

With respect to the Second Declaration of Dr. Polakis, submitted with Applicants' Preliminary Amendment filed July 5, 2006, the Examiner alleges that "There is no indication of *how much* the mRNA and protein was overexpressed, as there is no actual description of the experiment that was done, but rather a conclusory statement as to what was measured, and what it means" (Page 5 of the instant Final Office Action).

Dr. Polakis' statement that "an increased level of mRNA in a tumor cell relative to a normal cell typically correlates to a similar increase in abundance of the encoded protein in the tumor cell relative to the normal cell" is based on factual, experimental findings, clearly set forth in the Declaration. Accordingly, the Declaration is not merely conclusive, and the fact-based conclusions of Dr. Polakis would be considered reasonable and accurate by one skilled in the art. Further, the Examiner has not presented any convincing evidence to indicate that one of ordinary skill in the art would doubt the validity of PRO809 polypeptides have utility in the diagnosis of cancer.

The Examiner notes that Dr. Polakis is employed by the assignee. (Pages 4-5 of the instant Final Office Action).

Applicants note that the sworn Declaration of Dr. Polakis is sufficient to support Applicants' position that the gene amplification influences gene expression at the mRNA and protein levels.

The Examiner also alleges that the two Polakis declarations are not consistent. In particular, the Examiner alleges that in the first declaration, Dr. Polakis states that "approximately 200 gene transcripts that are present in human tumor **cells**……", while in the second declaration, He states that "approximately 200 gene transcripts that are present in human tumor **tissue**……" (Emphasis added). The Examiner also alleges that the second declaration uses the term "at mRNA level" and "at the protein level," which is different from the first declaration. The Examiner further alleges that it cannot determined whether these two declarations refer to the same data set, and there has not been any explanation of why the Declarant now refers to tumor tissue rather than tumor cells, nor what the perceived significance of this change is." (Page 5 of the instant Final Office Action)

Applicants respectfully disagree and fail to see how the two declarations are inconsistent and why the Examiner requires that the two declarations use the exact same wording. If a mRNA/protein correlation exists in tumor cells, most likely it will exist in tumor tissues. With respect to the use of the term "overexpression at mRNA level" and "overexpression at the protein level," Applicants submit that they are simply the rephrase of "increases in the level of a particular mRNA" and "increase in the level of a particular protein." Thus, contrary to the Examiner's allegation, the two declarations are consistent.

Taken together, despite some teachings in the art of certain genes that do not fit within this paradigm which are exceptions rather than the rule, in the vast majority of amplified genes, the combined teachings in the art as exemplified by Orntoft *et al.* and other references discussed and submitted in this case, as well as the Dr. Polakis Declaration, overwhelmingly teach that gene amplification influences gene expression at the mRNA and protein levels. Thus, one of skill in the art would reasonably expect, in this instance, based on the amplification data for the PRO809 gene, that the PRO809 protein is concomitantly overexpressed. Thus, Applicants submit that the PRO809 proteins have utility in the diagnosis of cancer and based on such a utility, one of skill in the art would know exactly how to use these molecules.

Further, Applicants would like to bring to the Examiner's attention a recent decision by the Board of Patent Appeals and Interferences (Decision on Appeal No. 2006-1469), in a microarray case. In its decision, the Board reversed the utility rejection, acknowledging that "there is a strong correlation between mRNA levels and protein expression, and the Examiner has not presented any evidence specific to the PRO1866 polypeptide to refute that." (Page 9). Applicants submit that, in the instant application, the Examiner has likewise not presented any evidence specific to the PRO809 polypeptide to refute Applicant's assertion of a correlation between mRNA levels and protein expression. Accordingly, Applicants respectfully request that the outstanding rejections be withdrawn and this case passed to issue.

In conclusion, Applicants have demonstrated a credible, specific and substantial asserted utility for the PRO809 polypeptides, for example, in detecting over-expression or absence of expression of PRO809. In fact, the art also indicates that, if a gene is amplified in cancer, it is **more likely than not** that the encoded protein will also be expressed at an elevated level. Based on these discussions, one skilled in the art, at the time the application was filed, would know how to use the claimed polypeptides. Hence, these data clearly support a role for PRO809 polypeptides, as a lung tumor marker.

Accordingly, the present 35 U.S.C. §101 and §112, first paragraph, utility rejections should be withdrawn.

II. Claim Rejections - 35 U.S.C. §112, First Paragraph - Enablement

Claims 122-126 and 129-131 stand further rejected under 35 U.S.C. §112, first paragraph, as allegedly "the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention." (Page 3 of the instant Final Office Action).

Applicants respectfully traverse this rejection. Based on the discussions above under utility for the PRO809 polypeptides in the diagnosis of lung cancer, Applicants submit that the skilled artisan would not require undue experimentation to make and use the claimed invention.

Accordingly, Applicants request that this rejection be withdrawn.

III. Claim Rejections Under 35 U.S.C. §103

Claims 122-126 and 129-131 are rejected under 35 U.S.C. 103(a) as being unpatentable over clone H74302 isolated by Hillier *et al.* (1995) in view of Sibson, WO94/01548. Applicants respectfully traverse and request reconsideration of this rejection and their arguments below.

Arguments

Applicants submit that, the prior art, Wash U-Merck EST H74302 sequence only disclosed a DNA sequence with about 90% DNA sequence homology to that of SEQ ID NO: 223. Contrary to the Examiner's assertion, Wash U-Merck EST H74302 did not possess or reduce to practice a DNA sequence identical to SEQ ID NO: 222 encoding for the PRO809 polypeptide.

More importantly, contrary to the Examiner's assertion, Hillier *et al.*, did not possess or reduce to practice the "complete" polypeptide sequence identical to the instantly claimed PRO809 polypeptide of SEQ ID NO: 223, nor did they teach or disclose how to obtain the polypeptide from the EST clone. One of skill in the art would not have been able to make a polypeptide of SEQ ID NO: 223 without first having realized that Wash U-Merck EST H74302 was part of a coding sequence, an act which would have required additional knowledge about the protein sequence to be used for the DNA extension, like prior knowledge of PRO809's extracellular domain, for instance. Such knowledge was not disclosed or even suggested by the

teachings of Hiller et al., (who did not disclose or reduce to practice the encoded polypeptide) around the effective filing date of the instant application. By merely looking at the Wash U-Merck EST H74302 DNA sequence, one would not know whether the sequence was a cDNA or whether it would code for any polypeptide, or for a part of a protein. The instantly claimed subject matter could not have been derived from the Wash U-Merck EST H74302 sequence alone, without significant work by the Applicants which would contribute towards "conception, completion and operation" of the invention. For instance, the instant specification discloses discussions on "cluster analysis" especially in Examples 1-3 and Example 118 of the specification. As explained in Example 1 of the specification:

> "The extracellular domain (ECD) sequences (including the secretion signal sequence, if any) from about 950 known secreted proteins from the Swiss-Prot public database were used to search EST databases. The EST databases included public databases (e.g., Dayhoff, GenBank), and proprietary databases (e.g. LIFESEQ^{TM}, Incyte Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST-2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)) as a comparison of the ECD protein sequences to a 6 frame translation of the EST sequences. Those comparisons with a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, WA)."

Using the approaches of ECD homology screening, clustering and assembly of EST fragments from public (e.g., GenBank) and/or private (LIFESEQ®, Incyte Pharmaceuticals, Inc., Palo Alto, CA) databases, and extension, Applicants identified clusters that contained DNA sequences encoding for full-length secretory polypeptides. These full-length DNA sequences were later isolated and cloned using PCR-based methods and such methods are described in detail in the Examples of the instant specification. Secretory polypeptide-encoding cDNA sequences were further identified in the nucleic acid sequences described above by applying a proprietary signal sequence finding algorithm developed by Genentech, Inc. (South San Francisco, CA). A brief explanation of how the signal sequence finding algorithm identifies a secretory polypeptide-encoding nucleic acid sequence is found in Example 3 of the instant specification. Since the signal sequence finding algorithm was proprietary, it was not available to one of ordinary skill in the art.

Applicants submit that even if it had been known that the Wash U-Merck EST H74302 sequence was a coding sequence, which Applicants strongly do not concede to, it would have

encoded for a different polypeptide from that of PRO809. This is evident from the alignment between the instant claimed PRO809 polypeptide (upper line throughout the alignment) and the putative translated Wash U-Merck EST H74302 polypeptide sequence (alignment enclosed in IDS). Applicants also enclose a copy of the translated polypeptide of the clone H74302 isolated by Hillier *et al.*, which produces a smaller protein sequence with 199 amino acids compared to that of PRO809 polypeptide with 265 amino acids. The Blast protein sequence alignments show a minimal sequence similarity of only 16 amino acids between PRO809 polypeptide and Wash U-Merck EST H74302 polypeptide sequence.

Taken together, Applicants submit that the instantly claimed polypeptide sequence could not have been derived from the Wash U-Merck EST H74302 sequence alone, without significant work by the Applicants which would contribute towards "conception, completion and operation" of the invention. Applicants used their own knowledge (clustering analysis, extension of DNA sequences and PCR-based cDNA library screening to obtain the full-length nucleic acid sequence encoding for the PRO809 polypeptide, etc.) and were the first to reduce to practice the PRO809 polypeptide of SEQ ID NO: 223. Further, even if the Wash U-Merck EST H74302 polypeptide sequence were supposedly reduced to practice, the sequence does not encode for the PRO809 polypeptide nor a polypeptide having at least 95% amino acid sequence identity to the PRO809 polypeptide of SEQ ID NO: 223. Accordingly, Hillier et al. do not teach or anticipate the polypeptides of Claims 122-126 and 129-131.

Further, the secondary reference Sibson et al. also do not teach or anticipate the instant invention. Therefore, this §103(a) rejection falls as neither reference teaches or anticipate the instantly claimed polypeptide.

Accordingly, neither of the cited references teach or anticipate the instant invention and thus, this rejection under 35 U.S.C. §103(a) should be withdrawn..

CONCLUSION

In conclusion, the present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited. Should there be any further issues outstanding, the Examiner is invited to contact the undersigned agent at the telephone number shown below.

We are requesting a three-month extension of time along with a Notice of Appeal and fees are due. The Commissioner is hereby authorized to charge any fees, including any fees for extension of time or Notice of Appeal, or credit overpayment to Deposit Account No. **08-1641**, referencing Attorney's Docket No. **39780-2630 P1C44**.

Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: October 2, 2007

By: _____
Panpan Gao (Reg. No. 43,626)
on behalf of Daphne Reddy (Reg. No. 53,507)

HELLER EHRMAN LLP
275 Middlefield Road
Menlo Park, California 94025-3506
Telephone: (650) 324-7000
Facsimile: (650) 324-0638

SV 2305630 v1
10/2/07 3:46 PM (39780.2630)